Editorials

Carbohydrate confusion[1]

Until recently, it was generally believed that the carbohydrates in our diet differed only in regard to their digestibility. A small proportion, less than 5% in the average diet, is not digested and so passes through the body unchanged. The remainder is digested to yield a variety of monosaccharides – almost entirely glucose, fructose and galactose – and then readily absorbed. Fructose and galactose, and the various small amounts of other sugars such as xylose and mannose that might be in the diet, were assumed to be rapidly converted into glucose. Thus, it was supposed that, soon after ingestion, all the digestible carbohydrate was circulating in the bloodstream as glucose. There was therefore no reason to expect any different reactions by the body to the different digestible dietary carbohydrates; they were all reduced to one common monosaccharide, the fate of which was to be metabolized so as to release energy, either immediately or after being stored as glycogen or fat.

These views of dietary carbohydrate are incomplete and erroneous, both in respect of the small indigestible fraction and in respect of the larger digestible fraction.

Nature of dietary carbohydrate

The small indigestible (unassimilable) part of the carbohydrate in the diet, together with the even smaller quantities of indigestible noncarbohydrate constituents, comprise what is generally known as dietary fibre.

The digestible carbohydrates contribute about 50% of the energy in the average British diet (National Food Survey Committee 1977). They amount to some 350 g per day, of which about 175 g is starch, 140 g sucrose ('sugar'), 20 g lactose and the remaining 15 g a mixture of glucose and fructose (Yudkin 1967). Starch is provided mostly in bread and other manufactured cereal foods, and in potatoes. The sucrose is almost entirely sugar extracted from the cane and beet, and is added to foods and drinks in the household, but to a greater extent to foods and drinks made by the food manufacturer. Lactose occurs almost exclusively in milk and milk products such as yoghourt; very little is found in most cheeses. The remaining small quantities of sugars, chiefly glucose and fructose and a little sucrose, are contained in fruit and vegetables.

In the diets of the poorer countries of Africa, Asia and South America, the total amount of carbohydrate tends to be only a little higher, perhaps 400 g per day (Yudkin 1964). But it differs qualitatively in three important respects. First, whereas in Western diets about 50% of the carbohydrate is starch and about 40% sucrose, in third world diets almost all of the carbohydrate is starch, and often 10% or less is sucrose. This small amount of sucrose occurs almost entirely in fruits and vegetables, rather than in manufactured foods and drinks to which sucrose is added. Secondly, the starch in Western countries is to a large extent derived from cereals consumed after a high degree of milling, so that much of the dietary fibre is removed. In many third world countries on the other hand the degree of milling is often much less, so that a greater amount of fibre is consumed. Thirdly, the consumption of milk and thus of lactose is very much lower in third world countries than in other countries (Food and Agriculture Organization 1971).

The effect of these differences upon human health has been much debated during the last quarter of a century. The least controversial effect is that of lactose in producing gastric disturbances and diarrhoea in some people, who are then said to have lactose intolerance (Simoons 1969). This can be demonstrated by the oral administration of 50 g or 100 g of lactose dissolved in water; with this test, lactose intolerance can be shown to exist in a very much higher proportion of people from third world countries (Bayless 1972). Nevertheless, lactose in milk produces less reaction than does lactose dissolved in water, so that most of the individuals with lactose intolerance are able to tolerate reasonable quantities of milk in their diets with no ill-effects (Protein Advisory Group 1972).

The role of the other carbohydrates in preventing or producing disease is much more

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0141–0768/78/0071–0551/$01.00/0

controversial. There are undoubtedly several diseases that, to a greater or lesser extent, are commoner in Western countries than in the poorer countries; as we have seen, there are also considerable differences both in the amounts of sugar (sucrose) in the diets and in the amounts of dietary fibre. It is then very tempting to suppose that these associations imply causes: that the higher prevalence of coronary heart disease, for example, in Western Europe than in rural Africa is due to the high quantity of sugar we consume, or alternatively to the lack of dietary fibre. These two different hypotheses tend to determine the way in which people subscribing to them classify the carbohydrates and the major foods that contain them. Those that take the view that lack of dietary fibre is an important cause of disease classify foods as unrefined and refined. The former include especially cereals that are milled only slightly if at all, but many workers also include raw and brown sugars in the category of unrefined. These contain no fibre, but are supposed to have virtues, including protection against the so-called diseases of civilization, because of the presence of the minute quantity of nutrients they may contain. This belief is then carried over to refined cereals, which are said to be undesirable not only because they lack dietary fibre but because, like refined sugar, they have also been deprived of nutrients. In summary, the division of dietary carbohydrates into refined and unrefined implies that the starch and the sucrose, which together constitute 90% of the dietary carbohydrate in both poor and wealthy countries, have identical effects in the body, and that it is only the presence or absence of associated substances – the fibre and perhaps some nutrients – that determine whether there is a low or a high risk of developing particular diseases.

Refined and unrefined

At this point, we should make clear what is implied by the terms 'refined carbohydrate' and 'unrefined carbohydrate' in relation to the average British diet. Specifically, what difference would it make to our intake of dietary fibre and nutrients if on the one hand the bread and the sugar we ate were all unrefined, and on the other if they were all refined.

Our average daily intake of bread is about 130 g, and of sugar about the same. If we changed all our bread from white refined to wholemeal unrefined, we should have a change in intake of fibre and nutrients as indicated in Table 1. In absolute terms, this would somewhat increase the intake of fibre, and substantially reduce the intake of calcium. But the nutritional significance of some of the changes is not clear cut. There is no reason to suppose, for example, that the lower content of riboflavin in white bread – a reduction by 4% of the recommended intake – results in a degree of deficiency, since the vitamin is well represented in the rest of the diet. The iron and nicotinic acid in cereal foods are not very well absorbed by the body, and moreover absorption of the iron from other foods is reduced when dietary fibre is increased; the apparent superior supply of these two nutrients in wholemeal bread is thus largely or entirely illusory. Similarly, the somewhat higher protein content of wholemeal bread is offset by the lower amount that is absorbed in the presence of dietary fibre. In effect, the only difference that might possibly be of consequence to man is the difference in the amount of fibre itself, and it is this that we shall be discussing later.

The figures in Table 1 make it evident also that it is incorrect to refer to bread simply as carbohydrate, whether refined or unrefined. Rather more than 12% of bread, on a dry weight basis, is

Table 1. Differences in daily intakes of nutrients in diets containing average amounts (130 g/day) of bread either entirely white (made from 72% extraction flour) or entirely wholemeal (made from 100% extraction flour)

	Protein (g)	Thiamine (mg)	Riboflavin (mg)	Nicotinic acid (mg)	Calcium (mg)	Iron (mg)	Fibre (g)
White bread	11.3	0.24●	0.06	2.2●	120●	2.4●	20
Wholemeal bread	11.9	0.28	0.13	4.5	35	3.5	27
Change	+0.6	+0.04	+0.07	+2.3	−85	+1.1	+7
Recommended daily intake (RDI)■	73	1.2	1.7	18	500	10	—
Increase or decrease (% of RDI) when bread changed from all white to all wholemeal	+0.8%	+3.3%	+4.1%	+13%	−17%	+11%	—

● Partly added as supplement to white flour

■ For middle-aged man of moderate activity (Department of Health and Social Security 1969)

protein, and it also contains vitamins and mineral elements, so that it is by no means a pure carbohydrate. If we refer to bread as carbohydrate, we should logically also refer to bananas, currants, dates and figs as carbohydrate; we might then refer to Barcelona nuts or coconuts as fat, and to milk as water.

As for sugar, refined carbohydrate should strictly speaking refer to the white sugar (sucrose) such as we have in our sugar bowls, and unrefined carbohydrate to the raw sugar that mostly is exported from the countries where sugar cane is grown and imported into the countries where it is then refined. Raw sugar contains some 96% sucrose, together with a small amount of moisture, other sugars and extraneous matter such as sand, earth, moulds, bacteria and possibly sugar lice. If one were to substitute this for all the white sugar that finds its way into the British diet, it would on average supply roughly these proportions of the body's needs of nutrients: 2% thiamine, 4% riboflavin, 6% calcium and 20% iron. But of course this is a completely unrealistic assessment, since something like 70% of our intake of sucrose is in manufactured foods such as confectionery, ice cream, soft drinks, cakes and biscuits, in which raw sugar is never used. The brown sugars that are used occasionally in the house and in manufacture have little or none of the nutrients, certainly far less than does raw sugar. In practice then it is virtually impossible to make the change from refined sugar to unrefined sugar in the quantities normally consumed, but even if it were possible the nutritional contribution would be extremely small. The only arguable advantage of insisting on taking unrefined raw sugar, and avoiding refined white sugar and the foods and drinks that are made with it, is that the amount of sucrose consumed is then likely to be very much less.

Simple and complex

Those that take the view that the way carbohydrates produce disease when diets are relatively rich in sucrose and poor in starch often refer to the former as 'simple sugars' and to the latter as 'complex carbohydrates'. Here the implication is that all sugars are equally harmful, and all polysaccharides equally innocuous. This makes the assumption that the body reacts in one and the same way to to the small molecules of glucose, fructose, lactose, maltose and sucrose, and in a different way to the large molecules of starch. However, there is an alternative explanation for the possible harmfulness of dietary sucrose, which is that it has specific actions not shared either by other sugars or by starch.

These different views and assumptions can be tested by seeking answers to the following questions. Are the differences in the prevalence of some diseases between wealthy and poor countries due, at least in part, to differences in the nature of the carbohydrate in the diets? If this is so, is it because of the removal of particular ingredients from some of the carbohydrate-rich foods – that is, the refining of these foods – or is it due to the increase in the consumption of sucrose at the expense of some of the starch?

Since the refining of cereal foods and the increase of sucrose consumption go hand in hand, the answers to these questions do not come from further epidemiological studies. Moreover, the inhabitants of affluent countries differ from those of poor countries in other dietary and nondietary ways, and even within one country there are differences in lifestyle between those who habitually eat brown bread and those who eat white.

It is then necessary to proceed from hypotheses derived from epidemiological study to the experimental testing of them. Thus, we have to ask rather different questions. Is there any difference produced in the body by the consumption of refined carbohydrates, lacking especially fibre, as compared with the consumption of unrefined carbohydrates? Alternatively, is there a difference produced in the body by the consumption of sucrose as compared with starch? If one or the other of these comparisons does reveal different effects, do they provide evidence that particular sorts of carbohydrate are involved in producing some of the diseases of affluence? Finally, if it transpires that the effects of sucrose are such as to indict it as a possible cause of the disease, are these specific to sucrose or are they shared by the other simple sugars that occur in our diets?

Effects of dietary fibre

A great deal has been written about the possible role of fibre in the prevention of a range of diseases, which include constipation, obesity, colonic cancer, coronary disease and diabetes (*Lancet* 1977). Much of the evidence is epidemiological, pointing to the association of these conditions with diets low in fibre and making the elementary but still common error of confusing association with cause. The only proven effects of dietary fibre are threefold. First, it increases the volume of faeces and sometimes the frequency of defaecation (Mitchell & Eastwood 1976); secondly, it relieves the symptoms of diverticulitis (Painter *et al.* 1972); and thirdly, it decreases the absorption of several mineral elements (McCance & Walsham 1948). The first effect, in itself, may be of great psychological significance but it is of somatic significance only in those who really do suffer from constipation. The second effect is certainly of value in the treatment of diverticulitis, but the fact that the administration

of dietary fibre relieves the symptoms of the disease is not in itself a proof that a low intake of dietary fibre is its cause. The third effect, the binding of some mineral elements so as to hinder their absorption, is likely to be a cause of the clinical deficiency of zinc seen in the Middle East (Rheinhold *et al.* 1972), and may play a part in the production of rickets in Asian immigrants in this country (Wills *et al.* 1972).

There is still disagreement whether the dietary fibre present in cereals lowers the concentration of plasma cholesterol (Connell *et al.* 1975). But even if it is assumed that a slight reduction is of clinical significance – an assumption that many observers would reject – there is no acceptable evidence that this would occur by an increase in dietary fibre by the amount that would result from a substitution of whole wheat flour for white flour in our bread. As we saw in Table 1, this substitution would increase our average dietary fibre from about 20 g to 27 g per day; substitution by the more commonly consumed brown bread would produce an increase of only 3 g per day.

As to the other conditions in which dietary fibre is claimed to have a preventive role, the results of experiment provide little support so far. For example, there is no evidence that the increase in cereal fibre that would result from a change from white bread to brown bread increases satiety, so as to reduce caloric intake and thus prevent or cure obesity.

Effects of sucrose

Since the increase in dietary sucrose in Western countries has been at the expense of part of the dietary starch, the relevant experiments are those in which diets are compared that differ only in the proportion that they contain of these two carbohydrates. There is now a great deal of evidence, accumulated especially during the past ten or twelve years, that the substitution of sucrose for all or part of the dietary starch produces a wide range of changes (Yudkin 1972, 1976). It is relevant to our discussion that in experiments with animals, the sucrose used was refined white sugar; the starch was pure starch and thus a far more highly refined carbohydrate than the white bread commonly included in this term. The differences that have been observed therefore have nothing to do with the presence or absence of dietary fibre.

Studies have been made with several species of experimental animals and with human subjects, and although the effects of sucrose differ quantitatively between species, many of them are qualitatively much the same. For example, there is always an increase in the concentration of the lipids in fasting blood; in the rat and in man, the increase is greater in triglyceride than in cholesterol (Al-Nagdy *et al.* 1970, Szanto & Yudkin 1969), whereas in the spiny mouse there is a very large increase in cholesterol and a smaller increase in triglyceride (Bruckdorfer, Worcester *et al.* 1974). The glucose tolerance at first improves, but with continued sucrose feeding it deteriorates (Cohen & Teitelbaum 1964); this is accompanied by the development of insulin resistance in the tissues (Bruckdorfer, Kang *et al.* 1974). There is also an increase in the concentration in fasting blood of uric acid (Turner 1972) and, in about 30% of human subjects, an increase in insulin and 11-OH-corticosteroid (Yudkin & Szanto 1970*a*), an increase in platelet adhesiveness (Yudkin & Szanto 1972), and a paradoxical behaviour in platelet electrophoretic mobility in the presence of adenosine diphosphate (Yudkin & Szanto 1970*b*). In experimental animals, a considerable change occurs in the activity of several enzymes concerned with lipid metabolism, in the direction of increasing triglyceride synthesis and storage (Aitken *et al.* 1967, Bruckdorfer *et al.* 1972). There is enlargement of the liver and of the kidney, the former due to both hypertrophy and hyperplasia (Kang *et al.* 1977*a*, Bender *et al.* 1972). Histological and biochemical examination of the kidney shows changes strongly resembling those seen in the glomerulonephrosis of diabetes (Kang *et al.* 1977*b*); the retina too shows diabetic-like abnormalities (Cohen *et al.* 1972).

The properties of sucrose provide evidence of its involvement in human disease. It is most obvious in regard to obesity, as is attested by the history of many obese patients. Much of the high consumption of sugar in Western countries is of items where it is combined with other calorigenic ingredients – flour, fat, cocoa – to make cakes and biscuits, chocolate, confectionery and ice cream. Mainly, people take these foods and sugary drinks in order to get the pleasure of palatability and not to satisfy hunger (Yudkin 1978). Moreover, the metabolic effects of sucrose tend towards greater fat storage than do those of starch.

Other diseases in which sucrose may play a part have been considered in detail elsewhere, but it is worth repeating some of the reasons for believing that it is one of the causes of coronary heart disease, and of diabetes. The characteristics of coronary heart disease are not only the common (though not universal) elevation of blood lipids, but also a diminished glucose tolerance, hyperuricaemia, increased adhesiveness and abnormal electrophoretic mobility of blood platelets, and an increase in the blood concentration of insulin and corticosteroid. All of these are produced by dietary sucrose in several animal species, as well as in 30% of male human subjects.

The evidence that dietary sucrose may be a cause

of diabetes includes its effects on glucose tolerance, on tissue insulin resistance, and on the structure of the kidney and retina. Moreover, since sucrose produces several effects that are characteristic of some of the abnormalities seen in both coronary heart disease and diabetes, it becomes possible to explain why there is a clinical link between these two diseases.

The final question is whether the different effects of sucrose as compared with those of starch are due to the former being a simple sugar, and the latter a complex carbohydrate. At present, this is largely an academic question, since these two carbohydrates between them account for 90% or so of our total carbohydrate intake. However, there is already a suggestion that sucrose will be increasingly replaced in our diets by invert sugar (a mixture of glucose and fructose) and to some extent by fructose alone. Present evidence suggests that most of the effects of sucrose are due in small part to its ease of digestion and absorption compared with starch, also in small part to its being a disaccharide, but chiefly to the fructose released when sucrose is digested (Bruckdorfer *et al.* 1972). The substitution of dietary sucrose by a fructose-rich alternative will be of no advantage in terms of health.

Conclusion

There are several diseases that are more common in wealthier countries than in poorer countries; the best known are dental caries, obesity, coronary heart disease and diabetes. The cause or causes of these diseases cannot be isolated on the basis of consideration of population epidemiology alone, since there are many dietary and nondietary differences between the populations of these different countries.

Attempts to identify differences in the carbohydrate portion of the diets as being involved in the aetiology of these diseases have been hindered by the use of phrases such as refined carbohydrate and unrefined carbohydrate, or complex carbohydrates and simple sugars. Experimental work has produced little evidence that supports the suggestion that if we ate wholemeal bread rather than white bread, we would reduce our chances of developing obesity, coronary heart disease or diabetes. On the other hand, many metabolic differences have been demonstrated between (refined) sucrose, and (refined) starch. These differences provide strong evidence that sucrose is involved in the causation of these diseases.

But whatever our views on the role of the various carbohydrate-rich foods that we eat, it would be less confusing and misleading if we specified clearly what it is we mean when we speak of the foods that contain carbohydrate. 'Starch' and 'sucrose' have precise meanings, and it is not difficult to discover the composition of wholemeal bread, white bread, potatoes and other carbohydrate-rich foods. On the other hand, the use of the phrases 'refined carbohydrate' and 'unrefined carbohydrate' conceals the considerable and important metabolic differences produced by starch and by sugar, and the use of the phrases 'complex carbohydrate' and 'simple sugars' conceals the considerable and important differences produced by the different sugars.

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Clinical pharmacology in the National Health Service

One of the major contributions which academic medicine has been able to make to the British National Health Service (NHS) has been to act as a breeding ground for emergent clinical specialties. Thus, modern cardiology, nephrology, gastroenterology, endocrinology and chest medicine have all developed out of university departments of medicine to become essential components of the NHS.

The latest offspring to come from this lair is clinical pharmacology. The specialty now has an independent academic base in most medical schools, with professorial chairs in twenty of them. In addition to their teaching and research responsibilities, clinical pharmacologists based at university hospitals provide clinical services to their local community. The value of their service contributions has led several groups (Royal College of Physicians 1974, Medico-Pharmaceutical Forum 1975, Committee of Professors 1978) and individuals (Godber 1974, Hunter 1975) to promulgate the concept that clinical pharmacologists should become an integral part of the NHS with consultants in the discipline at all district general hospitals. Indeed, a few enlightened area health authorities have already made such appointments, and several others are discussing the possibility of creating posts in the near future. Many people, however, are confused about the role of the non-teaching hospital clinical pharmacologist (Davies 1976, British Pharmacological Society 1978).

Physicians with special interests working at district general hospitals make three contributions to patient care. First, they provide acute general medical services to outpatients and inpatients. Secondly, they offer their colleagues and patients the benefit of their knowledge of the diseases in which they specialize. Thirdly, they all possess special skills or 'tricks', e.g. cardiac catheterization, haemodialysis, endoscopy, hormone assays, pulmonary function tests. Whilst specialties may try to justify their existence by reason of their 'trick', this is the least important of their contributions. Many of the techniques (haemodialysis, hormone assays, pulmonary function tests) are carried out by technicians or nurses, and the others are physical skills which require rather less manual dexterity than, for example, violin making! This view implies no disrespect to the achievements of those who catheterize coronary arteries and pancreatic ducts, but their most important contributions stem from the intellectual skills required to understand, diagnose and treat the diseases in which they specialize.

Clinical pharmacologists are also physicians with a special interest in the actions and effects of drugs in man (and particularly diseased man). They are therefore analogous to other physicians with special interests – such as gastroenterology, nephrology or endocrinology – and their service contributions can be similarly categorized. First, they are general physicians and the Specialty Advisory Committee on Clinical Pharmacology of the Joint Committee on Higher Medical Training (1975) pays particular attention to this aspect of their training: clinical pharmacologists in district general hospitals therefore expect to devote a considerable part of their time to the outpatient and inpatient care of acutely-ill patients. Secondly, clinical pharmacologists are able to provide advice on the diagnosis and management of a wide range of problems related to drug therapy (including drug toxicity, therapeutic failure, drug interactions, acute poisoning) by virtue of their special knowledge of drug action and drug handling in disease. Thus, just as there are patients with cardiac, endocrine or neurological problems, so there are patients with clinical pharmacological problems – problems which can often be solved by the rational application of knowledge of modern pharmacology, pharmacokinetics and drug metabolism. Third, clinical pharmacologists believe that a significant part of their service role should include the continuing medical education of their colleagues (both in hospital and in general practice) in drugs and drug therapy (Medico-Pharmaceutical Forum 1975, Binns 1975, Herxheimer 1976, Aagaard 1977).

What then are the clinical pharmacologist's special skills or 'tricks'? Some people assume that the 'trick' is to prescribe drugs, but if this were so